

CLAIMS

1. Mucopolysaccharide fraction obtainable from heparin or from fractions including heparinic constituents of molecular weights from 2,000 to 50,000, such as are obtainable by extraction from mammalian tissues, this fraction being characterized in that it is soluble in an aqueous-alcoholic medium (water-ethanol) having a titer of 55-61° GL, in that it tends to insolubility in a water-ethanol medium having a higher alcohol content, in that it is insoluble in pure alcohol, and in that it has a Yin-Wessler titer and a USP titer which are respectively in a ratio of at least equal to 2, notably at least 3, preferably higher than 6.     >

2. Mucopolysaccharide fraction according to Claim 1, characterized in that the ratio of its Yin-Wessler titer to its USP titer is higher than 10, even than 16.

3. Mucopolysaccharide fraction according to Claim 1 or Claim 2, characterized in that it is essentially formed from constituents whose molecular weights are less than 10,000.

4. Mucopolysaccharide fraction according to Claim 3, characterized in that it is essentially formed from constituents whose molecular weights are comprised between about 2,000 and about 8,000.

5. Mucopolysaccharide fraction according to any one of Claims 1 to 4, characterized in that in a gel-filtration operation on a column of gel of polyacrylamide and of agarose, in bead form, of the type marketed under the name ULTROGEL AcA 44, it passes after elution of a volume of 2.5 liters, dead volume not included, when the gel-filtration is conducted, at a flow rate of 200 ml/hour, and a column having a diameter of 100 mm and a height of 1 m and when the concentration of mucopolysaccharide and the volume of the solution placed on the column have been respectively 50 mg/ml and 37.5 ml, the essential of this fraction being notably contained in the 1.5 liters of eluate which then pass.

6. Mucopolysaccharide fraction according to any one of Claims 1 to 5, characterized in that it is constituted by that which, in a gel-permeation system on columns lined with silica with a granulometry of 10 to 100 microns, of 250 mm height and 9 mm diameter, characterized by a retention time of the order of 5.7 to 7.5, notably from 6.6 to 7.0 minutes in such column, when 50  $\mu$ l of a solution of 1.3 mg/ml of this fraction in a 0.02 M

Na<sub>2</sub>SO<sub>4</sub> buffer, having been placed on this column, there then followed the elution of said fraction with a flow rate of 3 ml/minute.

7. Mucopolysaccharide fraction according to any one of Claims 1 to 6, characterized by ratios of Yin-Wessler/USP titers exceeding 10, notably of the order of 13-16, and having Yin-Wessler titers higher than 130, notably from 135-160 units/mg.

8. Mucopolysaccharide fraction according to any one of Claims 1 to 7, characterized in that its constituents are in the state of salts of at least one physiologically acceptable metal, such as sodium or calcium.

9. Process for preparing a mucopolysaccharide fraction having Yin-Wessler and USP titers in a ratio higher than 2, notably than 3, characterized by:

- suspending in an aqueous-alcoholic medium of the water-ethanol type, having a titer comprised between about 55 and about 61° GL, preferably of the order of 58° GL, a substance based on heparin or heparinic constituents whose molecular weights range notably from 2,000 to 50,000, this substance having a reduced content of inorganic salts, preferably less than 1% by weight,
- separating the insoluble fraction and recovering the solution containing the dissolved mucopolysaccharide fraction, from which it can in its turn be separated,

notably by alcoholic precipitation, from the abovesaid aqueous-alcohol medium.

10. Process according to Claim 9, characterized by an additional fractionating step of the mucopoly-saccharide fraction previously recovered from the abovesaid aqueous-alcoholic medium and redissolved in water, which step consists of adding to this aqueous solution from 1 to 2 volumes of ethanol and from 10 to 100 g/l of sodium chloride and of collecting, on the one hand, the equally active precipitate formed and, on the other hand, the content remaining dissolved in the supernatant liquor, notably by a further alcoholic precipitation, and which constitutes a fractionation product whose Yin-Wessler and USP titers respectively are in a ratio still higher than that relative to the initial fraction, notably passing from a value of the order of 3 to a value of the order of 6 to 8.

11. Process according to Claim 9 or Claim 10, characterized in that the mucopolysaccharide fraction obtained is subjected to a gel-filtration, notably on polyacrylamide and agarose gel, in bead form, known by the tradename ULTROGEL AcA 44, of which the effective fractionating zone is situated between effective molecular weights of 4,000 to 60,000 ( for linear molecules).

12. Mucopolysaccharide fraction having physical, chemical and biological characteristics of those obtained by the application of the process according to any one of Claims 9 to 11.

13. Pharmaceutical composition, notably for the control of coagulation, of which the active principle is constituted by the mucopolysaccharide fraction according to any one of Claims 1 to 8 and 12.

14. Composition according to Claim 13, characterized in that it is in the form of a sterile injectable concentrated solution of this fraction, usable in therapeutics, for the control of blood coagulation, which solution contains from 1,000 to 100,000 IU (Yin-Wessler)/ml of the mucopolysaccharide fraction, preferably from 5,000 to 50,000, for example 25,000 IU/ml, when these solutions are intended for sub-cutaneous injection, or containing again, for example from 500 to 10,000, for example 5,000 IU/ml of the mucopolysaccharide fraction, when it is intended for intravenous injection or for perfusion.

15. Biological reactant constituted by the mucopolysaccharide fraction according to any one of Claims 1 to 8 and 12.